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Evaluation and Management of Pulmonary Hypertension in Noncardiac Surgery: A Scientific Statement From the American Heart Association

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ABSTRACT: Pulmonary hypertension, defined as an elevation in blood pressure in the pulmonary arteries, is associated with an increased risk of death. The prevalence of pulmonary hypertension is increasing, with an aging population, a rising prevalence of heart and lung disease, and improved pulmonary hypertension survival with targeted therapies. Patients with pulmonary hypertension frequently require noncardiac surgery, although pulmonary hypertension is associated with excess perioperative morbidity and death. This scientific statement provides guidance on the evaluation and management of pulmonary hypertension in patients undergoing noncardiac surgery. We advocate for a multistep process focused on (1) classification of pulmonary hypertension group to define the underlying pathology; (2) preoperative risk assessment that will guide surgical decision-making; (3) pulmonary hypertension optimization before surgery to reduce perioperative risk; (4) intraoperative management of pulmonary hypertension to avoid right ventricular dysfunction and to maintain cardiac output; and (5) postoperative management of pulmonary hypertension to ensure recovery from surgery. Last, this scientific statement highlights the paucity of evidence to support perioperative pulmonary hypertension management and identifies areas of uncertainty and opportunities for future investigation.

Key Words: AHA Scientific Statements ■ hypertension ■ pulmonary ■ prevalence ■ pulmonary surgical procedures ■ ventricular dysfunction

Pulmonary hypertension (PH) is a heterogeneous group of disorders that result in an elevation in blood pressure in the pulmonary arteries (mean pulmonary artery [PA] pressure [mPAP] >20 mm Hg).[1] Increased mPAP is consistently associated with an increased risk of death.[2] The prevalence of PH is increasing, with an aging population, a rising prevalence of heart and lung disease, and improved PH survival with targeted therapies.[3] Patients with PH frequently require noncardiac surgery. In a large nationwide study from the United States, PH was reported in 0.81% of cases, with an increasing prevalence from 0.4% in 2004 to 1.2% in 2014.[4] Despite the rising prevalence of PH among patients undergoing noncardiac surgery, there is scant guidance on perioperative management.[5,6] This scientific statement provides a framework and clinical guidance for the evaluation and management of PH in patients undergoing noncardiac surgery.

OVERVIEW OF PH

PH can result in right-sided heart failure (RHF) with unique pathophysiology. This is most notable in pulmonary arterial hypertension (PAH), an obliterative pulmonary vasculopathy characterized by endothelial and smooth muscle cell proliferation. This leads to destruction of and abnormal angiogenesis and concomitant pulmonary arterioles with a progressive increase in pulmonary vascular resistance (PVR). The increasing afterload on the right ventricle (RV) results in the phenomenon of RV-to-pulmonary vascular uncoupling, and if uncoupling remains untreated, RHF may ensue (see the Pathophysiology of RHF in PH).[7]

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Table 1. Clinical and Hemodynamic Classifications of PH

Clinical classification of PH		
1 PAH		
1.1 Idiopathic PAH		
1.1.1 Nonresponders at vasoreactivity testing		
1.1.2 Acute responders at vasoreactivity testing		
1.2 Heritable PAH		
1.3 Drug- and toxin-induced PAH		
1.4 PAH associated with:		
1.4.1 Connective tissue disease		
1.4.2 HIV infection		
1.4.3 Portal hypertension		
1.4.4 Congenital heart disease		
1.4.5 Schistosomiasis		
1.5 PAH with features of venous/capillaries (PVOD/PCH) involvement		
1.6 Persistent PH of the newborn		
2 PH associated with left-sided heart disease		
2.1 Heart failure		
2.1.1. With preserved ejection fraction		
2.1.2 With reduced or mildly reduced ejection fraction		
2.2 Valvular heart disease		
2.3 Congenital/acquired cardiovascular conditions leading to postcapillary PH		
3 PH associated with lung diseases or hypoxia		
3.1 Obstructive lung disease or emphysema		
3.2 Restrictive lung disease		
3.3 Lung disease with mixed restrictive/obstructive pattern		
3.4 Hypoventilation syndrome		
3.5 Hypoxia without lung disease (eg, high altitude)		
3.6 Developmental lung disorders		
4 PH associated with chronic PA obstruction		
4.1 Chronic thromboembolic PH		
4.2 Other PA obstructions		
5 PH with unclear or multifactorial mechanisms		
5.1 Hematological disorders		
5.2 Systemic disorders		
5.3 Metabolic disorders		
5.4 Chronic renal failure with or without hemolysis		
5.5 Pulmonary tumor thrombotic microangiopathy		
5.6 Fibrosing mediastinitis		
Hemodynamic Classification of PH		
Definitions	Hemodynamics	Clinical group
Precapillary PH	mPAP >20 mm Hg PAWP ≤15 mm Hg PVR >2 WU	1, 3, 4, 5
Isolated postcapillary PH	mPAP >20 mm Hg PAWP >15 mm Hg PVR ≤2 WU	2, 5
Combined precapillary and postcapillary PH	mPAP >20 mm Hg PAWP >15 mm Hg PVR >2 WU	2, 5
Exercise PH	mPAP/CO slope between rest and exercise >3 mm Hg·L^{-1}·min^{-1}	1, 2, 3, 4, 5

CO indicates cardiac output; mPAP, mean pulmonary artery pressure; PA, pulmonary artery; PAH, pulmonary arterial hypertension; PAWP, pulmonary arterial wedge pressure; PCH, pulmonary capillary hemangiomatosis; PH, pulmonary hypertension; PVOD, pulmonary veno-occlusive disease; PVR, pulmonary vascular resistance; and WU, Wood units.

Adapted from Humbert et al[10] with permission from the European Society of Cardiology and European Respiratory Society.

Hemodynamic Classification

The classification of PH has evolved over the years from the 1973 World Health Organization symposium[8] to the 6th World Symposium on Pulmonary Hypertension (WSPH)[9] in 2018 and the European Society of Cardiology/European Respiratory Society guidelines for the diagnosis and treatment of PH,[10] which decreased the PH threshold from an mPAP ≥25 mm Hg to an mPAP >20 mm Hg (2 SDs above the mPAP of a healthy patient at rest, 14.0±3.3 mm Hg[11]), differentiated PH on the basis of PVR >2 Wood units (instead of ≥3 Wood units),[10] added granularity to the traditional group 1 to 5 classifications, included a hemodynamic definition for exercise PH,[10] and provided more detailed hemodynamic classifications of precapillary and postcapillary PH (Table 1). However, limitations with these hemodynamic definitions remain, which are based on a single time point without standardization of provocative challenges to assess vasoreactivity, lack of clarity on the ideal preload, and potential erroneous measurements and accuracy of pulmonary capillary wedge pressure across the respiratory cycle.[12] Nevertheless, use of this classification framework is essential for the best management strategies for patients with PH.

Clinical Classification

It is important to recognize that the WSPH clinical classification system covers a spectrum of different diseases that can cause PH, and many patients may cross these groups with multiple contributors to their PH.[13] WSPH group 1 PH includes idiopathic PAH, hereditary PAH (with type II bone morphogenetic protein receptor making up 80% of identified mutations), PAH associated with connective tissue disease, congenital heart disease (procedurally corrected or uncorrected), portal hypertension, HIV, drug-induced PAH (now more commonly seen with methamphetamines compared with previous decades when it was commonly associated with anorexigenic drug use) and schistosomiasis (the most common cause of PAH worldwide). Within WSPH group 1, significant differences exist in profiles and management strategies between different patient subtypes. Patients with vasodilator-responsive PAH display long-term responsiveness to calcium channel blockers with hemodynamic stability and near-normal RV function. In contrast, patients with congenital heart disease and high mPAPs can display chronic desaturation, erythrocytosis, and severe RV dysfunction. Patients with scleroderma pan-vasculopathy can have abnormal pulmonary function tests (with overlaps of group 3 PH) and more impaired RV function.[10] Also included in WSPH group 1 are patients with pulmonary veno-occlusive disease and pulmonary capillary hemangiomatosis, who, it is important to note, may develop pulmonary edema in response to PAH-targeted therapies as a result of postcapillary pulmonary venous remodeling.[10]

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WSPH group 2 includes patients with pulmonary venous hypertension secondary to left ventricular (LV) systolic heart failure, heart failure with preserved LV ejection fraction, valvular heart disease, cardiomyopathies (hypertrophic, restrictive, or infiltrative), and atrial myopathies.[14] Hemodynamically, these patients fall into profiles of isolated postcapillary PH, in which disease involvement is limited to the left side of the heart, and combined precapillary and postcapillary PH, which can also involve remodeling of the pulmonary vasculature. Differentiating combined precapillary and postcapillary PH in the setting of heart failure with preserved LV ejection fraction from PAH with secondary LV diastolic abnormalities can be challenging and is often associated with comorbidities of obesity, sleep apnea, hypertension, diabetes, older age, anemia, and chronic renal failure. Pathological changes may include both pulmonary arterial and venous proliferation[15] but the absence of the plexogenic arteriopathy from systemic-to-PA collaterals that is characteristic of PAH.[16]

WSPH group 3 comprises patients with lung diseases, including various hypoxic lung diseases, which have different pathophysiological mechanisms. Chronic obstructive pulmonary disease, interstitial lung diseases, obesity and hypoventilation, prior pneumonectomy, long-term high-altitude exposure, and regional hypoxemia of the lung parenchyma may lead to PH in a susceptible and perhaps genetically predisposed patient. Hypoxic pulmonary vasoconstriction is an adaptive mechanism specific to the lung vasculature that temporarily improves ventilation/perfusion matching; hypoxic pulmonary vasoconstriction in the chronic setting may become maladaptive and promote PH with vascular remodeling.[17] Various hypoxic lung diseases may be associated with PH and have different pathophysiological mechanisms that are associated with PH. Whereas PH associated with chronic obstructive pulmonary disease may have frank vascular dropout on angiography, interstitial pulmonary fibrosis is associated with remodeling of the small pulmonary arteries, capillaries, and venules.[18] Interstitial lung diseases associated with systemic sclerosis, connective tissue disease (which display overlap with group 1 PH), and some of the nonspecific interstitial pneumonias may display vascular proliferation with an increase in intimal and adventitial thickness and a decrease in the number of blood vessels.[17]

WSPH group 4 includes patients with PH attributable to chronic thromboembolism and other pulmonary arterial obstructions.[19] PH attributable to chronic thromboembolism is the most common of these diseases and is caused by persistent obstruction of the pulmonary arteries by organized thrombi from unresolved acute pulmonary embolism and scarring of the pulmonary vasculature in response to that insult.[20] The risk factors for PH attributable to chronic thromboembolism are similar to those for acute pulmonary embolism but also include specific factors such as a history of splenectomy and non-O blood group.[20] PH attributable to chronic thromboembolism has several treatment options, with potentially curative pulmonary thromboendarterectomy surgery and other therapies such as balloon pulmonary angioplasty and medical therapy shown to improve PH. However, even after successful pulmonary thromboendarterectomy, some patients will have PH.[19] These patients may still display small-vessel disease similar to PAH, with reactive prethrombotic occlusion, postocclusion with remodeling, or reactive vasoconstriction in unaffected areas of the lung.[21]

Last, WSPH group 5 includes diagnoses with multifactorial mechanisms that do not fit into the other PH categories. These multifactorial mechanisms include systemic illnesses such as sarcoidosis, renal failure, hemoglobinopathies, and myeloproliferative diseases.[10] The clinical and hemodynamic classifications of PH by WSPH group are shown in Table 1.

PAH-Targeted Therapies

Many therapies, referred to as PAH-targeted or specific therapies, have been developed to address the abnormal pulmonary vascular remodeling seen in PAH. Although frequently referred to as pulmonary vasodilators, these drugs have complex mechanisms of action, including antiproliferative effects.[22] Currently, 3 classes of targeted therapies are approved by the US Food and Drug Administration for the treatment of group 1 PH[10]:

- Nitric oxide (NO) pathway mediators: phosphodiesterase 5 (PDE5) inhibitors: tadalafil and sildenafil; soluble guanylate cyclase stimulator: riociguat.
- Endothelin receptor antagonists: bosentan, ambrisentan, and macitentan.
- Prostacyclin pathway agonists: prostacyclins: treprostinil (oral, inhaled, subcutaneous, or intravenous), iloprost (inhaled), and epoprostenol (intravenous or inhaled); oral prostaglandin I2 receptor agonist: selexipag.

For non–group 1 PH, the mainstay of treatment is focused on targeting the underlying disease, for example, heart disease in group 2 PH or lung disease in group 3 PH. In group 2 PH, no clear role has been demonstrated for PAH-targeted therapies.[10] In fact, PDE5 inhibitors have been shown to be detrimental in patients with persistent PH after left-sided heart valvular surgery.[23] In group 3 PH, inhaled treprostinil has been shown to be beneficial in interstitial lung disease–associated PH.[24] In chronic thromboembolic pulmonary hypertension, riociguat is approved by the US Food and Drug Administration to treat nonoperative chronic thromboembolic pulmonary hypertension,[25] with evidence for efficacy of macitentan[26] and subcutaneous treprostinil.[27] In group 5 PH, PDE5 inhibitors have been shown to increase the risk of painful crises in PH associated with sickle cell

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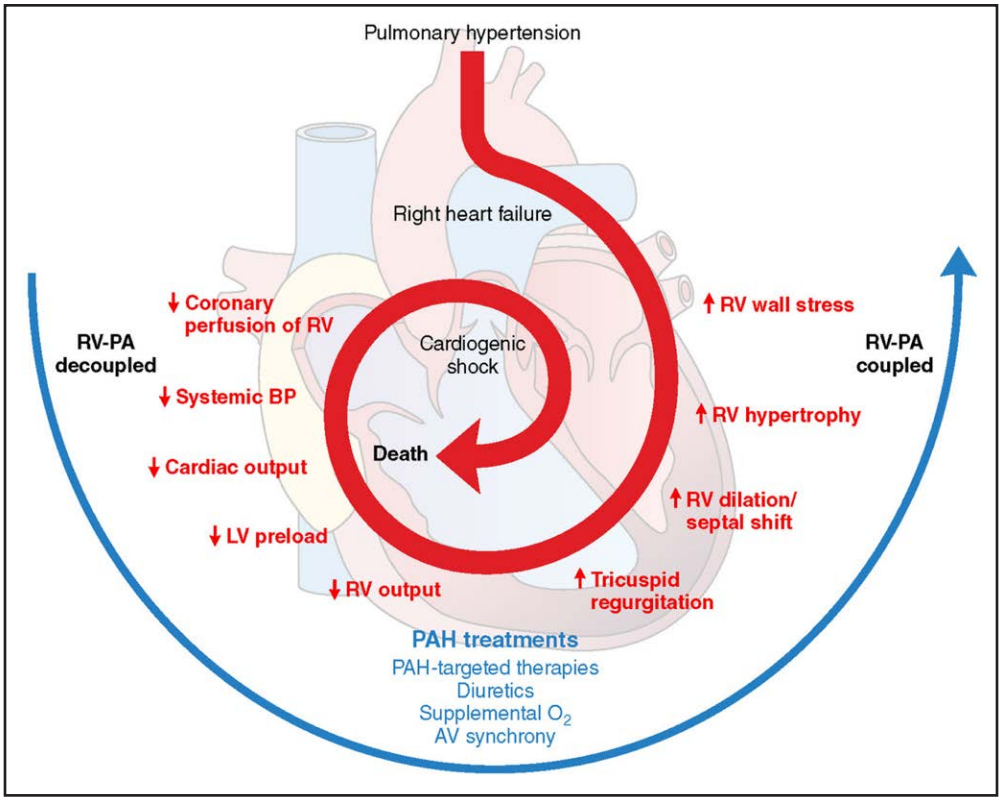

Figure 1. Worsening of right-sided heart failure in PH.
Initially in response to increase right ventricular (RV) wall stress in pulmonary hypertension (PH), the RV compensates through hypertrophy and maintaining RV–pulmonary artery (PA) coupling. With progression of PH, the resulting RV dilatation and tricuspid regurgitation promote a downward spiral (red arrow) attributable to worsening RV afterload mismatch, tricuspid regurgitation, systolic function, and ischemia that results in decompensation (RV-PA decoupling), right-sided heart failure, and cardiogenic shock. Treatments, including pulmonary arterial hypertension (PAH)–targeted therapies, diuretics, supplemental O_2, restoration/maintenance of atrioventricular (AV) synchrony, and iron repletion, can all counteract (blue arrow) the downward spiral of RV failure in PH. BP indicates blood pressure; and LV, left ventricular.

disease.[28] PAH-targeted therapies have been associated with benefit in observational studies of sarcoid-associated PH.[29,30] In selected patients who have multiple contributors to their PH that includes a group 1 component, there may be a role for PAH-targeted therapies.[13]

PATHOPHYSIOLOGY OF RHF IN PH

Although defined by specific hemodynamic criteria, PH is further characterized by the functional status of the right side of the heart.[12] Under normal physiological circumstances, the pulmonary circulation is highly compliant, creating a low-resistance system to facilitate blood flow from the RV. The RV free wall is typically thin (<5 mm) and has significantly less myocardial mass than the LV in the setting of normal physiology. In PAH, a high PVR results in increased RV wall stress, leading to cardiac myocyte hypertrophy, increased wall thickness, and augmented contractility. These changes initially maintain stroke volume, albeit limited by maximum RV hypertrophy. With disease progression, the RV dilates, leading to inefficient energy transfer in contractility. This loss of RV contractile function ultimately leads to an uncoupling of the pulmonary circulation from RV contractility, which is no longer matched to its afterload. Over time, this progression results in the development of RHF, which encompasses RV and right atrial (RA) dysfunction, tricuspid valve regurgitation, and loss of atrioventricular synchrony.[31] Severe RV dilation is associated with interventricular dependence and septal shift, compromising LV performance and thus further contributing to a reduced stroke volume and decreased coronary perfusion.

Increases in RV wall stress, hypertrophy, dilation, and dysfunction raise myocardial metabolism, oxygen consumption, and coronary perfusion (Figure 1). Increased wall stress and thickness require increased myocardial oxygen consumption; however, RV hypertrophy lengthens the diffusion distance from capillaries to myocytes, limiting oxygen supply.[32] To compensate, there must be either an increase in oxygen extraction or improved mechanical efficiency of the myocardium. RV perfusion is proportional to the pressure gradient between the aorta and RV throughout the cardiac cycle. In PH with RHF, this gradient is reduced, further limiting effective coronary perfusion.[33] To compensate, an increase in oxygen extraction or improved mechanical efficiency of the myocardium is necessary. There is

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a maladaptive shift in metabolism from free fatty acids to glucose in the failing RV, but the rate of glucose uptake is not increased sufficiently to compensate for the reduced efficiency of RV mechanics and oxygen utilization, leading to further worsening of right-sided heart function.[7,32] Together, these physiological changes can lead to a downward spiral of RHF that can ultimately crescendo into cardiogenic shock and death (Figure 1).

The pathophysiology of RV remodeling in PAH is also linked to genetic and hormonal features. Type 2 bone morphogenetic protein receptor mutations are associated with worsening RHF through lipotoxicity relative to comparable levels of RV afterload in individuals without this mutation.[7] Estrogen improves RV function and bioenergetics through multiple mechanisms in PH, including reduced inflammatory cytokine expression and proapoptotic signaling. Thus, male compared with female patients with similar PVR elevation tend to have a blunted RV ejection fraction improvement with PAH treatment.[7,34]

Although therapy for PH is generally directed at the pulmonary arterial circulation, the ultimate goal is to optimize the performance of the right side of the heart (Figure 1). Diuretics reduce filling pressures and wall stress, thus optimizing efficiency and RV coupling to the pulmonary circuit.[31,35] Supplemental oxygen and iron repletion will enhance the content of hemoglobin and myoglobin and support myocardial energy metabolism.[31] In addition, maintenance of normal sinus rhythm with atrioventricular synchrony is paramount for optimal RV function, hemodynamics, and prognosis in PAH.[36,37] PAH-targeted therapies, including endothelin receptor antagonists, PDE5 inhibitors, soluble guanylate cyclase stimulators, and prostacyclin pathway agonists, which are all frequently used in combination, improve RV function and clinical outcomes in PAH.[38] The goal of PAH-targeted therapies is to achieve low-risk clinical status defined by parameters that reflect RV performance such as clinical heart failure, syncope, functional capacity, BNP (B-type natriuretic peptide) or NT-proBNP (N-terminal pro-BNP) levels, RV size and function by echocardiography or magnetic resonance imaging, RA pressure (RAP), and cardiac index.[10,35] This approach to optimizing RV performance should similarly be applied to PH management to minimize perioperative risk in noncardiac surgery.

PERIOPERATIVE RISK OF PH IN NONCARDIAC SURGERY

PH is associated with excess morbidity and death in patients undergoing noncardiac surgery, with increased risks of heart failure, cardiac arrhythmias, hemodynamic instability, respiratory failure, prolonged ventilatory support, and intensive care. Studies evaluating the risks of PH in patients undergoing noncardiac surgery are presented in Table 2.[4,39–53] In a study of 17 million hospitalizations for major noncardiac surgery in the United States from 2004 to 2014, perioperative major adverse cardiovascular events, including death, myocardial infarction, or stroke, were 4-fold higher in patients with a diagnosis of PH compared with those without PH (8.3% versus 2.0%; $P<0.001$).[4] Patients with PH were older, less likely to be women, and more likely to have a history of smoking, chronic pulmonary disease, obstructive sleep apnea, and valvular heart disease than those without PH. After adjustment for demographics, clinical comorbidities, and surgery subtypes, PH was associated with a 43% increased odds of the composite end point of death, myocardial infarction, or stroke (adjusted odds ratio, 1.43 [95% CI, 1.40–1.46]) and a nearly 2-fold higher risk of cardiogenic shock and cardiac arrest.[4] In the subset of patients with a diagnosis code for PH (2.4% of surgical inpatients with any diagnosis of PH), major adverse cardiovascular events occurred in ≈13% of surgical hospitalizations. Compared with patients in this population without PH, those with a PH diagnosis had a 2- to 3-fold increase in major adverse cardiovascular events after adjustment for demographics and clinical characteristics (adjusted odds ratio, 2.51 [95% CI, 2.26–2.79]).[4]

A prospective, international, multicenter, observational study of patients with PAH (WSPH group 1) undergoing nonobstetric, noncardiac surgery at 11 specialized PH centers reported major complications in 6.1% and perioperative mortality rate in 3.5% of patients.[47] Mortality rate was 15% in emergency procedures compared with 2% in nonemergency surgeries. Risk factors for major perioperative complications were an elevated RAP ≥7 mm Hg before surgery, decreased 6-minute walking distance, and the perioperative use of vasopressors (perhaps signaling poor preoperative optimization, perioperative care needs, or a combination of these potential scenarios). In addition, several single-center studies have provided valuable insights into the surgical risks associated with PH. In one retrospective analysis of 1276 adult patients undergoing noncardiac surgery with general anesthesia between 1991 and 2003, 145 patients displayed precapillary PH (WSPH group 1, 3, or 4) and a mean RV systolic pressure of 68±21 mm Hg as measured by echocardiography. Furthermore, perioperative complications occurred in 42% of these cases.[41] Other complications included respiratory failure (28%), cardiac arrhythmias (12%), acute congestive heart failure (11%), acute renal insufficiency (7%), septic shock (7%), and postoperative mortality rate (7%). Univariate predictors of postoperative death in this cohort included prior pulmonary embolism, electrocardiographic right-axis deviation, echocardiographic evidence of RV hypertrophy or an RV index of myocardial performance by echocardiography ≥0.75, a ratio of RV systolic pressure to systemic systolic blood pressure ≥0.66, and

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Table 2. Studies Evaluating Risks of PH in Patients Undergoing Noncardiac Surgery

	Ammash et al,[39] 1999	Krowka et al,[40] 2000	Ramakrishna et al,[41] 2005	Minai et al,[42]	Lai et al,[43] 2007	Memtsoudis et al,[44] 2010	Price et al,[45] 2010	Kaw et al,[46] 2011	Meyer et al,[47] 2013	Bennett et al,[48] 2014	Kim et al,[49] 2014	Seyfarth et al,[50] 2015	Pathak,[51] 2017	Díaz-Gómez et al,[52] 2018	Smilowitz et al,[4] 2019	Deljou et al,[53] 2020
Years enrolled	1988–1996	1996–2000	1991–2003	1996–2002	1999–2004	1998–2006	2000–2007	2002–2006	2007–2010	1991–2011	2003–2008	2011–2014	2000–2010	2006–2016	2004–2014	2010–2017
Patients with PH, n	24	43	145	21	62	Not reported	28	96	114	33	115	16	33	37	Not reported	131
Surgeries, n	28			28		THA, 1359 TKA, 2184				53					693 819	
Age, y	29	≈41.5±14.7	60.1±16.0	47±20	67±15	THA, 74 TKA, 72	53±15	62.4±11.5	57 (48–67)	24	73.3±10	≈66.0±8.2	66	62.5±13.2	71.6±14.6	59±14.9
Female, %	71	≈67	73	57	39	THA, 68 TKA, 72	57	50	70	Not reported	69	63	75	78	63	77
WHO group PH included	Eisenmenger physiology/ primary congenital heart disease	Group 1 (portopulmonary hypertension)	Groups 1, 3, 4	All subtypes (II, 38%; III, 57%; IV, 5%)	All subtypes	All subtypes	Groups 1, 4	All subtypes	Group 1	Eisenmenger physiology/ primary congenital heart disease	All subtypes	Groups 1, 3, 4	All subtypes	Groups 1, 3, 4, 5	All subtypes	Groups 1, 3, 4
PA pressures, mmHg	Not reported	mPAP 49±14	Mean PASP 68±21	mPAP 53±14.4	Mean PASP 78.8±9.4	Not reported	mPAP 43±12	Mean RVSP 49.4±20.6	mPAP 45 (38–55)	Median PASP 100 (75–117)	Not reported	mPAP 39.3±6.1	Mean PASP 80.2	Mean RVSP 68.3±62	Not reported	mPAP 25-40 in 43%; 41–55 in 38%; >55 in 20%
Surgery type	Noncardiac	Liver transplantation	Noncardiac	Noncardiac	Noncardiac	Orthopedic	Noncardiac	Noncardiac	Noncardiac	Noncardiac	Orthopedic	Orthopedic	Noncardiac	Noncardiac	Noncardiac	Noncardiac
Anesthesia type	Not reported	Not reported	GETA (100%)	GETA (79%) Other (21%)	GETA (58%) Regional (34%) MAC (8%)	Not reported	GETA (50%) Regional (50%)	GETA (100%)	GETA (82%) Regional (18%)	GETA (72%) MAC (24%) Regional (4%)	Regional (99%)	GETA (75%) Regional (25%)	GETA (91%) Regional (9%)	MAC (51%) GETA (43%) Regional (5%)	Not reported	GETA (98%) MAC (2%)
No. of centers	Multicenter	Multicenter	Single center	Single center	Single center	Multicenter	Single center	Single center	Multicenter	Single center	Single center	Single center	Single center	Single center	Multicenter	Single center
Study design	Retrospective								Prospective	Retrospective						

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Table 2. Continued

	Ammash et al,[39] 1999	Krowka et al,[40] 2000	Ramakrishna et al,[41] 2005	Minai et al,[42]	Lai et al,[43] 2007	Memtsoudis et al,[44] 2010	Price et al,[45] 2010	Kaw et al,[46] 2011	Meyer et al,[47] 2013	Bennett et al,[48] 2014	Kim et al,[49] 2014	Seyfarth et al,[50] 2015	Pathak,[51] 2017	Díaz-Gómez et al,[52] 2018	Smilowitz et al,[4] 2019	Deljou et al,[53] 2020
	Case series	Case series	Case series	Case series	Cohort study	Cohort study	Case series	Cohort study	Survey	Case series	Cohort study	Case series	Cohort study	Case series	Cohort study	Case series
Adverse outcomes reported	Death	Death	Heart failure; myocardial ischemia or infarction; stroke; respiratory failure; hepatic dysfunction; renal insufficiency; sepsis or hemodynamic instability; cardiac arrhythmias; death	Acute renal failure; aspiration pneumonia; RHF; sepsis; postoperative death	Myocardial infarction or ischemia; stroke; heart failure; major arrhythmia; delayed extubation; death	Acute respiratory distress syndrome; pulmonary embolism; deep vein thrombosis; death	Severe acute RHF requiring vasopressors, inotropes, inhaled NO or additional pulmonary vasodilator therapy; hypoxia requiring an escalation of the mode of ventilation; isolated hypotension or RV failure not requiring vasopressors or inotropes; death	Heart failure; myocardial infarction; respiratory failure; hemodynamic instability; sepsis; death within 30 d; hospital length of stay; and 30-d readmission	Major bleeding (EBL >1 L); systemic inflammatory response or septicemia requiring catecholamine therapy; RHF requiring inotropic support; in-hospital death	Death	Respiratory complications; cardiac arrhythmias; heart failure; myocardial ischemia or infarction; pulmonary embolism; fat embolism syndrome; altered mental status; death	RHF; bleeding; infection; delayed wound healing; arrhythmia, death	Myocardial infarction; stroke; heart failure; arrhythmias; delayed extubation >24 h	Myocardial ischemia or infarction; cardiac arrhythmias; heart failure; respiratory failure; prolonged ventilator support >48 h postoperatively; RV failure; sepsis; acute kidney injury; hepatic dysfunction; death	Myocardial infarction; stroke; in-hospital death	Heart failure; dysrhythmia/atrial fibrillation; hypotension requiring vasopressors; cardiac arrest; pneumonia; acute respiratory distress syndrome; respiratory failure; pulmonary edema; pneumothorax; delirium; stroke; acute kidney injury; shock; sepsis; bleeding; reoperation; 30-d death
Death, %	7	35	7	18	10	THA, 2.4 TKA, 0.9	7	1	4	4	0	6	9	5	4.4	3
Morbidity, %	Not reported	Not reported	42	19	24	Not reported	29	28	6	Not reported	35	38	9	28	8.3	27

EBL indicates estimated blood loss; GETA, general endotracheal *anesthesia*; MAC, monitored anesthesia care; mPAP, mean pulmonary artery pressure; NO, nitric oxide; PASP, pulmonary artery systolic pressure; PH, pulmonary hypertension; RHF, right-sided heart failure; RV, right ventricular; RVSP, right ventricular systolic pressure; THA, total hip arthroplasty; TKA, total knee arthroplasty; and WHO, World Health Organization.

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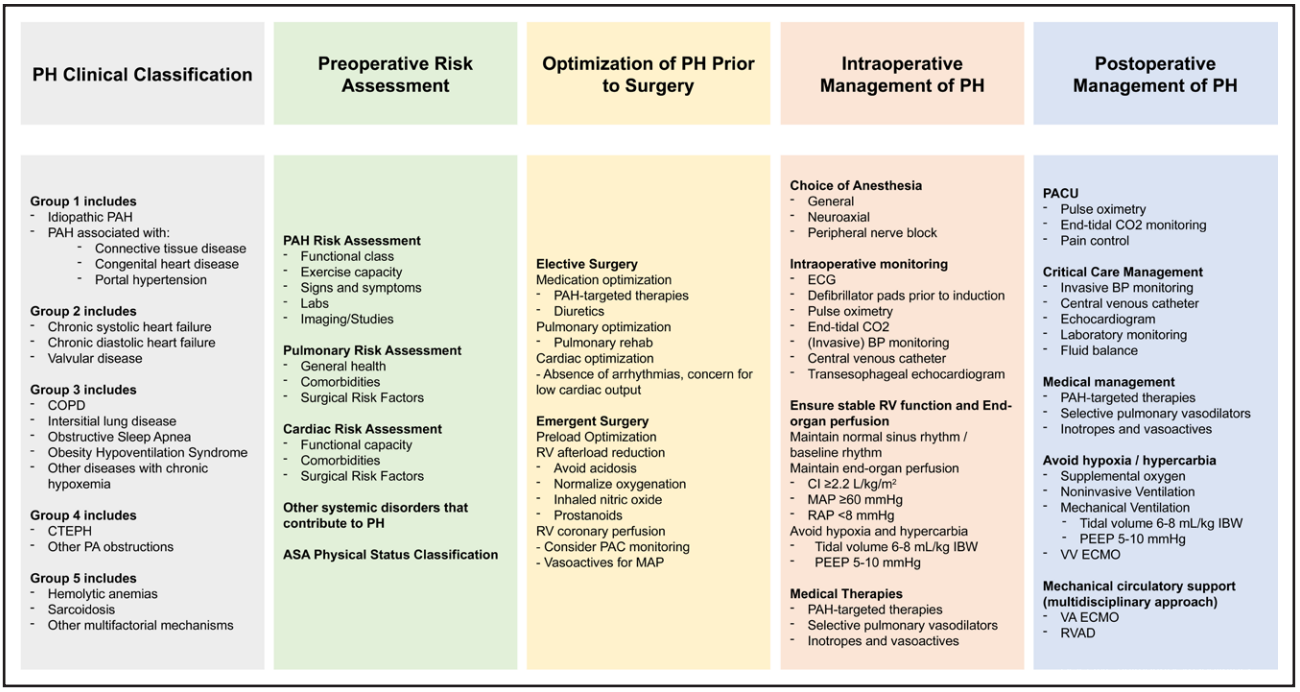

Figure 2. Overview of management of PH in noncardiac surgery.
Management of pulmonary hypertension (PH) first requires a diagnosis with the World Symposium on Pulmonary Hypertension (WSPH) clinical classification (gray). Some patients may have aspects of multiple WSPH groups and require more complex management (Table 1 provides more details on PH classification). This clinical classification then guides the preoperative risk assessment (green) based on contributors to their PH and overall health status (Figure 3 provides more details). This classification guides optimization of PH before surgery, especially with regard to pulmonary artery (PA) hypertension (PAH)–targeted therapies and preload optimization (yellow). Such optimization is limited in the setting of emergency surgery, where rapidly acting pulmonary vasodilators and vasoactive therapies may be used. In the intraoperative management of PH (pink), decisions must be made about the choice of anesthesia and intraoperative monitoring. The goal is to ensure stable right ventricular (RV) function and end-organ perfusion; some guidance is provided on specific hemodynamic goals, although these may differ depending on the clinical context. In the postoperative setting (blue), patients may recover quickly after care in the postanesthesia care unit (PACU), whereas others may require critical care because of complications from surgery or right-sided heart failure. ASA indicates American Society of Anesthesiology; BP, blood pressure; CI, cardiac index; COPD, chronic obstructive pulmonary disease; CTEPH, chronic thromboembolic pulmonary hypertension; ECMO, extracorporeal membrane oxygenation; IBW, ideal body weight; MAP, mean arterial pressure; PAC, pulmonary artery catheter; PEEP, positive end-expiratory pressure; RAP, right atrial pressure; RVAD, right ventricular assist device; VA, venoarterial; and VV, venovenous.

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intraoperative use of vasopressors.[41] Another study of 131 patients with precapillary PH who underwent 196 noncardiac surgeries under general anesthesia from 2010 to 2017 identified perioperative complications in 27% of patients.[53] Specifically, perioperative cardiovascular complications occurred in 16% of cases, cardiac arrhythmias in 11%, hypotension requiring vasopressors in 7%, heart failure in 3%, and cardiac arrest in 1%; mortality rate at 30 days was 3%. In covariate-adjusted analyses, intermediate- or high-risk noncardiac surgery, worse World Health Organization functional class, and elevated NT-proBNP concentrations (≥300 pg/mL) in patients with PH were independently associated with perioperative complications.[53]

Comparisons of perioperative outcomes of noncardiac surgery by mechanism and severity of PH have not been fully explored. The available evidence is derived from observational data, and substantial uncertainty remains about the risks of noncardiac surgery in patients with PH. Hemodynamic characteristics that correlate with postoperative risk have yet to be elucidated, and validated risk scores are needed to identify surgical patients at the greatest risk for complications.

PREOPERATIVE RISK ASSESSMENT IN PH

The general approach to perioperative management of PH in noncardiac surgery is outlined in Figure 2. After determination of the patient's type(s) of PH, an individualized risk assessment for perioperative complications should be performed.[5] Table 3 summarizes surgical and nonsurgical clinical risk assessment tools for PH and other comorbidities, including heart disease and lung disease relevant to patients with PH.[5,10,54–61] Patient-related factors include PAH, meeting high-risk criteria, evidence of RV dysfunction, obstructive sleep apnea, a low exercise capacity, and an American Society of Anesthesiology physical status classification of 2 or greater.[4,5,46,47,62,63] American Society of Anesthesiology physical status classification of 2 or greater includes patients with non–life-threatening severe systemic

Table 3. Comparison of Common Nonsurgical and Surgical Risk Assessment Tools for Patients With PH and Other Comorbidities

PAH risk assessment (intermediate- and high-risk features)			
Tool	REVEAL 2.0[54,55]	European Society of Cardiology/Respiratory Society guideline-derived risk assessment[55a]	FPHR[55b]/COMPERA[55c] (included in COMPERA but not FPHR)
Functional class	≥III	≥III	≥III
Exercise	6MWD (<440 m)	6MWD (<440 m), CPET (peak VO_2 <15 mL·min^{-1}·/kg^{-1} (<65% predicted), VE/VCO_2 slope >36)	6MWD <440 m
Signs and symptoms	SBP <110 mm Hg, HR >96 bpm	Clinical signs of progressive RV failure, syncope	
Laboratory values	BNP >50 ng/L NT-proBNP >300 ng/L	BNP >50 ng/L NT-proBNP >300 ng/L	BNP >50 ng/L NT-proBNP >300 ng/L
Hemodynamics/imaging	Echocardiogram (pericardial effusion) PFT (DLCO <40% predicted) Right-sided heart catheterization (mRAP >20 mm Hg, PVR >5 WU)	Echocardiogram (pericardial effusion) Cardiac MR (RA area >18 cm^2) Right-sided heart catheterization (RAP >8 mm Hg, CI <2.4 L·min^{-1}·m^{-2}, SvO_2 <65%)	RAP ≥8 mm Hg CI ≤2.4 L·min^{-1}·m^{-2}* SvO_2 ≤65%*
PH mechanism	PAH associated with connective tissue disease, heritable PAH, portopulmonary PH	WHO group I (PAH)	
Comorbidities	Renal insufficiency		
Demographics	Males age >60 y		
Pulmonary risk assessment			
Tool	ARISCAT[56]	Arozullah respiratory failure index[57]	Gupta calculator for postoperative respiratory failure[58]
General health	Preoperative oxygen saturation <95%, age >51 y	Age >60 y, partially/fully dependent	Partially/fully dependent, ASA class >2
Comorbidities	Respiratory infection in the last month, anemia (hemoglobin <10)	Preoperative serum creatinine >2.0 mg/dL, history of severe chronic obstructive pulmonary disease, albumin <3g/dL	Systemic sepsis within 48 h before surgery
Surgical risk factors	Emergency case, location of surgical incision (upper abdominal, intrathoracic), duration of surgery (>2–3 h)	High-risk type of surgery (abdominal aneurysm, thoracic, neurosurgery, upper abdominal, neck), emergency case	High-risk type of surgery, emergency case
Cardiac assessment			
Tool	2014 AHA/ACC guidelines[59]	Revised cardiac risk index[60]	Vascular Quality Initiative Cardiac Risk Index[61]
General health	Functional capacity <4 METs		Age >70 y
Comorbidities	Unstable cardiac conditions (unstable coronary syndromes, decompensated heart failure, atrial arrhythmias, ventricular arrhythmias, severe valvular disease)	History of ischemic heart disease, congestive heart failure, cerebrovascular disease, insulin treatment, creatinine >2 mg/dL	History of ischemic heart disease, heart failure, insulin treatment, creatinine >2 mg/dL, abnormal stress test
Surgical risk factors	Emergency surgery, high- or intermediate-risk surgery (aortic and other major vascular surgery, peripheral artery surgery, carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic surgery, orthopedic surgery, prostate surgery)	High- or intermediate-risk surgery (aortic and other major vascular surgery, peripheral artery surgery, carotid endarterectomy, head and neck surgery, intraperitoneal and intrathoracic surgery, orthopedic surgery, prostate surgery)	Prior vascular procedure

PAH risk assessments have not been validated in noncardiac surgery, and full details on calculations of risk scores are available in the cited references.

AHA/ACC indicates American Heart Association/American College of Cardiology; ASA, American Society of Anesthesiology; BNP, brain natriuretic peptide; CI, cardiac index; COMPERA, Comparative, Prospective Registry of Newly Initiated Therapies for Pulmonary Hypertension; CPET, cardiopulmonary exercise test; DLCO, lung-diffusing capacity for carbon monoxide; FPHR, French Pulmonary Hypertension Registry; HR, heart rate; MET, metabolic equivalent; MR, magnetic resonance; mRAP, mean right atrial pressure; NT-proBNP, N-terminal probrain natriuretic peptide; PAH, pulmonary arterial hypertension; PFT, pulmonary function test; PH, pulmonary hypertension; PVR, pulmonary vascular resistance; RA, right atrial; RAP, right atrial pressure; REVEAL, Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management; RV, right ventricle; SBP, systolic blood pressure; 6MWD, 6-minute walking distance; WHO, World Health Organization; and WU, Wood units.

disease or greater and individuals with poorly controlled diabetes or hypertension, chronic obstructive pulmonary disease, morbid obesity (body mass index ≥40 kg/m^2), moderate reduction of LV ejection fraction, and end-stage renal disease on hemodialysis.[66] Obstructive sleep apnea may be associated with PH and can be screened for with the STOP-Bang (snoring, tiredness, observed apnea, blood pressure, body mass index, age, neck size, gender) questionnaire.[67] Procedure-related risk factors include emergency surgery, intermediate- to high-risk surgery, intraoperative need for vasopressors, and prolonged surgery beyond 3 hours.[5,41,47,62,63]

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Patients with intermediate- to high-risk PH have a higher risk of perioperative complications than patients with mild disease.[41] Even low-risk procedures have an increased risk of major adverse cardiovascular events in patients with PH compared with patients without PH.[4] The risk is attributed to an increased incidence of decompensated heart failure, hemodynamic instability, myocardial infarction, stroke, dysrhythmias, respiratory failure with prolonged mechanical ventilatory support leading to prolonged stay in intensive care unit (ICU), and increased death.[4,5,44–47,49]

Whenever feasible, preoperative evaluations by an anesthesiologist and a PH specialist should be performed. However, in an emergency situation, consulting with a PH specialist before transport to the operating room may not be possible. Thus, an anesthesiologist with experience in PH should lead the perioperative care of these patients. Diagnostics can include a formal transthoracic echocardiogram (TTE) performed by a cardiac sonographer or a cardiac point-of-care ultrasound examination done by a clinician proficient or board certified in cardiac ultrasonography to assess right-sided heart function and to provide relevant information for immediate clinical risk stratification. For elective surgeries, there should be a clear multidisciplinary discussion of the urgency and need for the operation before surgical planning.[63] Patients with a known PH diagnosis may undergo right-sided heart catheterization or TTE during preoperative planning for elective noncardiac surgery. Other patients may not have a formal diagnosis of PH but may present with suspicious signs (abnormalities on chest imaging such as a dilated PA or contrast reflux into the internal vena cava) or symptoms (exertional dyspnea, syncope, or presyncope) during preoperative planning. TTE is the standard of care to identify high-risk features of PH such as RV dilation, RV dysfunction, tricuspid valve regurgitation jet velocity >2.8 m/s, flattened interventricular septum on the parasternal short-axis view, RA enlargement, and pericardial effusion.[69,70] Patients with high-risk features generally warrant comprehensive cardiopulmonary risk assessments by a multidisciplinary group of physicians.[59,62,71] Patients who display evidence of acute RHF should be medically managed for hemodynamic optimization before consideration for noncardiac surgery.

Under rare circumstances, mechanical RV support may be considered for severe RV systolic failure before noncardiac surgery. The decision to use this approach should carefully consider hematological and systemic effects.[5] For example, use of a percutaneous RV assist device could be a thoughtful approach to managing preoperative severe RV systolic failure in the setting of low PVR and normal LV ejection fraction. However, this mechanical approach may be inappropriate in the setting of untreated severe precapillary PH because the RV assist device will not improve RV pressure overload[72] and may paradoxically induce more RV dysfunction[73] by increasing the risk of lung injury, pulmonary hemorrhage, hypovolemic shock, and low cardiac output.[72,74] In contrast, venoarterial (VA) extracorporeal membrane oxygenation (ECMO) support may be used as a bridge to heart-lung transplantation or RV myocardial recovery with the benefit of unloading both the right side of the heart and the pulmonary circulation.[73,74] Thus, a comprehensive multidisciplinary discussion is essential to coordinate the most appropriate treatment strategy for these patients.

We propose a general preoperative pathway for patients with PH undergoing noncardiac surgery (Figure 3). The patient's initial preoperative risk assessment will directly affect surgical decision-making. Patients with intermediate- or high-risk PH could benefit from the expertise of an experienced anesthesiologist and perioperative care team[63] who are proficient in high-risk medical management, mechanical circulatory support, and transesophageal echocardiography when appropriate. For patients at intermediate or high risk undergoing elective surgery, the procedure should ideally be performed in a specialized PH center by clinicians familiar with the perioperative and intraoperative care of patients with PH.[5,63] Most PH centers can provide emergent mechanical circulatory support in the event of cardiovascular collapse from PH-induced RHF.[5] Patients who cannot be transferred to a specialized PH center could benefit from remote consultation from a PH specialist.[5]

OPTIMIZING PATIENTS WITH PH FOR SURGERY

Two to 4 weeks before surgery is a reasonable time frame for a patient visit to determine which components of risk stratification will be relevant at the time of surgery. These may include diagnostic testing and functional status. Symptoms (eg, progressive dyspnea or syncope) or signs (eg, elevated jugular venous pressure or peripheral edema) suggestive of acute heart failure predict morbidity and death.[75] Repeat TTE, ECG, laboratory tests (eg, creatinine, BNP/NT-proBNP), and 6-minute walking distance should be obtained and a cardiopulmonary exercise test and right-sided heart catheterization considered[76] because these data objectively determine the current health of the right side of the heart. Worse functional class[41,45] and shorter 6-minute walking distance preoperatively portend a 4-fold increase in perioperative complications.[45] Furthermore, the development of supraventricular tachycardia is an independent risk factor for death in patients with PH and should be treated.[77–79] Any sign indicative of suboptimal disease control mandates action: diuresis, advancement of targeted PH

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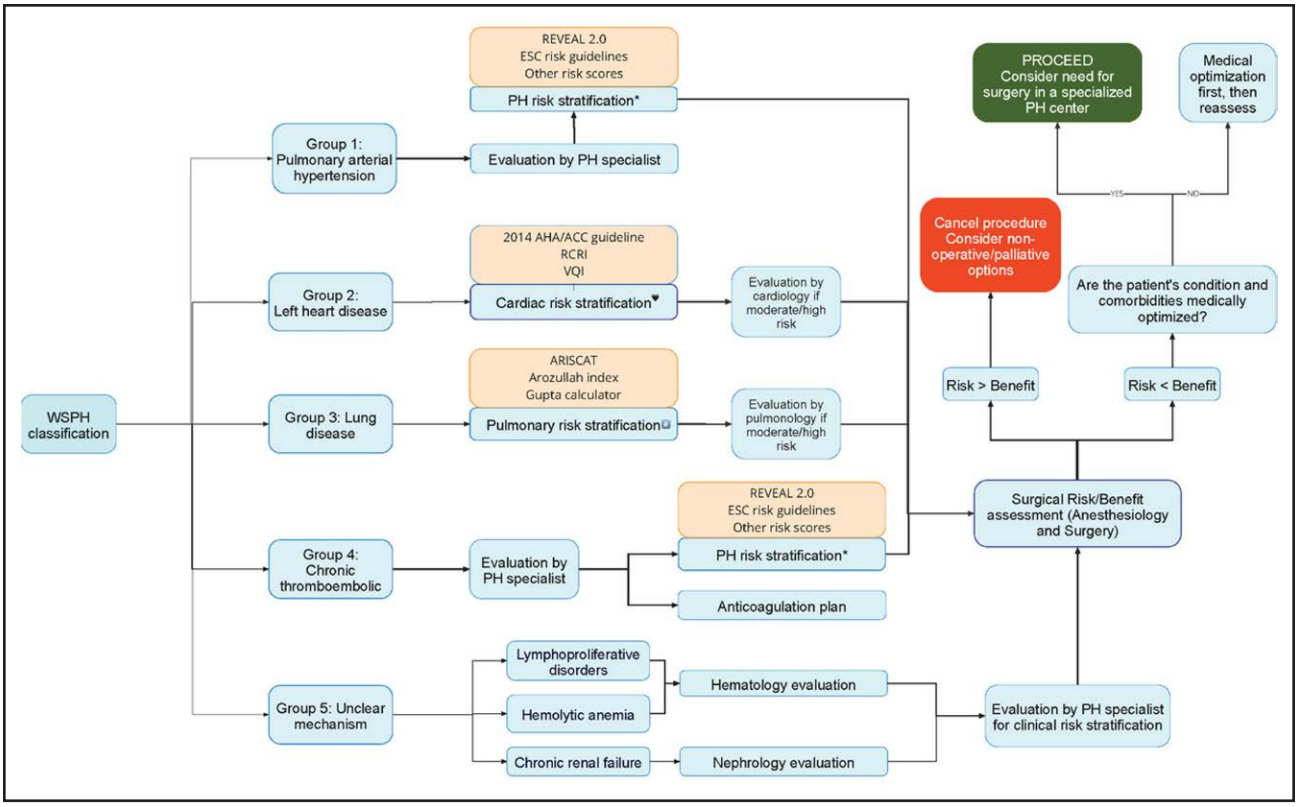

Figure 3. Algorithm for the perioperative assessment of the patient with PH.
Pulmonary hypertension (PH) risk can be estimated with multiple risk assessments, although none have been validated specifically for PH in noncardiac surgery. Medical PH risk assessments include the United States Registry to Evaluate Early and Long-Term Pulmonary Arterial Hypertension Disease Management (REVEAL 2.0) risk calculator,[54,55] the European Society of Cardiology (ESC)/Respiratory Society guideline-derived risk assessment,[55a] and other pulmonary arterial hypertension (PAH) risk scores derived from them.[55b,55c] Cardiac risk assessment can be performed with the 2014 American College of Cardiology/American Heart Association (ACC/AHA) guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery,[59] the revised cardiac risk index (RCRI),[60] or the Vascular Quality Initiative (VQI) Cardiac Risk Index for vascular surgery.[61] Pulmonary risk assessment can be performed with the ARISCAT (Assess Respiratory Risk in Surgical Patients in Catalonia) Risk Index,[56] the Arozullah respiratory failure index,[57] or the Gupta calculator for postoperative respiratory failure.[58] There are no formal risk calculator scores in group 4 PH, but chronic pulmonary thromboembolism is considered a high-risk feature for noncardiac surgery. Several causes can contribute to group 5 PH, which may require a multidisciplinary evaluation that includes a PH specialist to estimate clinical risk. Some patients undergoing elective noncardiac procedures may benefit from a preoperative echocardiogram and right-sided heart catheterization to guide risk assessment. The input from a PH specialist will be of value in determining the need for such additional testing,[63,74a] as well as working with the anesthesiologist and surgeon to estimate surgical risk. If the decision is to proceed, the surgery should ideally occur in a center specialized in PH if the surgery is determined to be intermediate or high risk.[74b] If the risk from the procedure exceeds the benefit, then the surgery would likely be postponed (until the patient's condition is optimized to a point where performing the surgery is feasible and safe) or canceled for consideration of nonsurgical/palliative options. WSPH indicates World Symposium on Pulmonary Hypertension.

therapy, afterload reduction, arrhythmia management, and, rarely, consideration for inotropic support of the RV. If targeted therapies are initiated before surgery, 6 to 12 weeks is usually adequate for allowing maximal therapeutic effects on the pulmonary vasculature before surgery.[10]

Pulmonary optimization is also critical for patients with PH. Hypoxia and acidosis can acutely and adversely affect PVR[80]; thus, an updated assessment of gas exchange by arterial blood gas analysis and pulse oximetry is prudent. Preoperative pulmonary function testing may uncover new or progressive restriction, obstruction, or both. A severely reduced diffusing capacity (<32% predicted[81]) may signify advanced PH and encourage the perioperative team to re-examine RV function or hemodynamics. A review of chest imaging such as PA and lateral chest x-rays within the preceding 3 to 6 months can identify parenchymal disease requiring further diagnostics or therapeutics. Pulmonary rehabilitation, which significantly improves quality-of-life scores, 6-minute walking distance, and even survival for patients with PH,[82,83] might be recommended before surgery to maximize the patient's recovery potential.

Attention to medication regimen maintenance before surgery is critical to ensure therapeutic stability. Interruption of most prostanoid therapies can lead to a rebound PH crisis that can be associated with significant morbidity and death.[84,85] Generally, patients should continue all targeted therapies up to and on the day of surgery,

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although some medications may need to be substituted (oral prostacyclin pathway agonists transitioned to parenteral or inhaled). Oral medications can be taken on the morning of surgery, even if there is a nothing-per-mouth order, to ensure intraoperative hemodynamic stability. Postoperatively, endothelin receptor antagonists cannot readily be crushed and administered through a nasogastric tube, but a liquid suspension of bosentan is available. Oral prostanoids often need to be transitioned temporarily to intraoperative inhaled or parenteral prostanoids while patients refrain from taking anything by mouth after surgery.[86] Patients with chronic thromboembolic PH may warrant bridging with anticoagulation because they are at heightened risk for thromboembolic complications. All patients with PH should be reminded to take their diuretics before surgery to avoid acute decompensated heart failure in the perioperative period.

INTRAOPERATIVE MANAGEMENT OF PH

Intraoperative Hemodynamic Goals

Intraoperative hemodynamic goals in patients with PH focus on preventing acute RV dysfunction and maintaining cardiac index to ensure adequate end-organ perfusion.[63,87,88] The following recommendations can provide general guidance to aid in achieving these goals. Practitioners are encouraged to personalize patient care goals by using the principles of this general guidance:

1. Avoid systemic hypotension (maintaining mean arterial pressure [MAP] ≥60 mm Hg if needed to ensure stable end-organ perfusion)[89] to ensure coronary perfusion and the prevention of RV ischemia. Data to recommend specific agents are lacking, although drugs that promote pulmonary vasoconstriction without promoting RV inotropy, for example, phenylephrine, should generally be avoided.
2. Maintain normal sinus rhythm. Patients should continue outpatient β-blockers and calcium channel blockers before surgery, but initiation intraoperatively should generally be avoided because of the negative inotropic effects.[90] Rapid restoration of sinus rhythm with electric cardioversion should be strongly considered in patients with new-onset hemodynamically significant arrhythmias. All patients with PH should have defibrillator pads applied before induction. In rare instances, temporary pacing, either transcutaneous or transvenous pacing, may be necessary after electric cardioversion. Alternatively, antiarrhythmic medical therapy can be initiated to attempt to restore and maintain sinus rhythm while monitoring for changes in RV contractility.
3. Avoid or mitigate factors known to increase PVR such as hypoxia, hypercarbia, acidosis, hypothermia, and pain.[91–94]
4. Avoid high airway pressures and positive end-expiratory pressure (PEEP). These parameters can be titrated for optimal gas exchange, hemodynamics, and RV function. A reasonable starting point is a tidal volume of 6 to 8 mL/kg ideal body weight, PEEP of 5 to 10 mm Hg, respiratory rate titrated to a Pa_{CO_2} of 30 to 35 mm Hg, pH >7.4, and fraction of inspired oxygen titrated to Sp_{O_2} >92%. PVR is lowest at functional residual capacity and has a U-shaped relationship with lung volumes. PVR and pulmonary pressures rise at low lung volumes, because of decreased tension in extra-alveolar arterioles, and at high lung volumes, because of compression of alveolar capillaries.[95,96] Inadvertent high PEEP from bag-mask ventilation in patients at risk for hyperinflation, for example, those with chronic obstructive pulmonary disease, can cause acute reductions in ventricular preload and severe hypotension.[97]
5. Maintain baseline RV loading conditions. Hypovolemia will cause a reduction in MAP and RV perfusion, whereas hypervolemia will cause RV overload and increased wall tension, compromising RV function. The hypertrophied RV can have a relatively narrow range of optimal preload,[98] and volume overload tends to be poorly tolerated.
6. Optimize central venous pressure, preload, and RV function with diuretics and PAH-targeted therapies. Ideally, such optimization was performed in the preoperative setting, but acute changes in the intraoperative period may require titration of these therapies. In the intraoperative setting, inhaled (NO or prostacyclin) or parenteral (subcutaneous or intravenous prostacyclin) PAH-targeted therapies can be used to acutely reduce RV afterload. An immediate hemodynamic effect can also be obtained by changing body position (eg, the Trendelenburg position and leg lift will acutely increase preload, whereas the reverse Trendelenburg position will lead to an acute reduction in preload), although the effect of diuretics may be delayed.
7. After optimization with diuretics and PH therapies, augmenting RV contractility and cardiac output with inotropic support and enhancing pulmonary vasodilation to reduce PVR may be warranted to maintain adequate end-organ perfusion by promotion of RV–to–pulmonary vascular coupling. The benefit of inotropes should be weighed against the risk of developing arrhythmias, which may be hemodynamically detrimental. Systemic vasodilators that reduce both PVR and systemic vascular resistance (SVR) may reduce RV perfusion pressure as a result of systemic hypotension.

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Intraoperative Monitoring

Intraoperative monitoring recommendations for patients with PH are based on expert opinion with limited evidence-based guidance for specific monitoring strategies and outcomes.[88,98–100] Standard American Society of Anesthesiology monitoring should be used in all patients,[100a] along with continuous invasive arterial blood pressure monitoring with an indwelling catheter. Clinician preference often dictates the timing of arterial line placement, which may occur before or after the induction of general anesthesia, depending on myriad factors (eg, baseline RV function, resting systemic or mixed venous oxygenation, predilection to dysrhythmias with transient hypotension). In cases with neuroaxial anesthesia (eg, epidural or spinal deposition of local anesthetic) alone or with general anesthesia, the decision for invasive monitoring with an arterial line depends on considerations similar to those in general anesthesia. If preload is not optimized, neuroaxial anesthesia together with decreased preload may decrease SVR profoundly. However, when general anesthesia includes neuromuscular blockade and controlled ventilation, the neuroaxial technique may be paired with a monitored anesthesia care approach during surgery (ie, intravenous administration of a sedative-hypnotic agent such as propofol).[63,98] Although patients may be spontaneously ventilating with a natural airway, obstruction or hypoventilation should be avoided given the adverse impact that hypoxia and hypercarbia impose on pulmonary vascular tone and RV function. Regional anesthetic techniques that do not affect the neuroaxis (ie, regional or peripheral nerve blocks) are often paired with the monitored anesthesia care approach, and similar considerations of airway obstruction and hypoventilation highlighted previously apply. When available and feasible, transesophageal echocardiography allows real-time assessment of biventricular function and estimation of PA systolic pressure through determination of RV systolic pressure, which is the sum of the RAP and the pressure gradient between the RA and RV. This echocardiographic modality can be considered for intraoperative hemodynamic monitoring in patients undergoing major, prolonged, and high-risk surgeries under general anesthesia.[101] For transesophageal echocardiography use, most clinicians prefer a protected airway with an endotracheal tube to avoid aspiration of stomach contents, along with stimulation of the upper airway, which can become a problem with the monitored anesthesia care approach. Furthermore, the scheduled operation may not allow transesophageal echocardiography use (ie, esophagectomy), and an alternative approach should be considered with TTE if feasible.

The decision to use central venous catheters (with or without a PA catheter [PAC]) for invasive monitoring and vasoactive medication administration should be based on (1) the severity of RV dysfunction and PH, (2) the level of surgical risk (ie, risk of significant hemodynamic disturbances), and (3) the anesthesiologist's expertise in interpreting the obtained data.[102] Although a static value of central venous pressure does not predict preload status, the dynamic intraoperative changes are useful for assessment of changes in RV filling pressure and detection of new-onset RHF or worsening tricuspid valve regurgitation (eg, loss of x descent, with fusion of c and v waves and large v wave). Hypotension in the setting of an increased central venous pressure may signify worsening RV function and the need for inotropic support, whereas hypotension with decreased central venous pressure most often suggests reduced preload and the need for intravascular volume expansion. Preinduction central venous catheter placement can be obtained whenever the need for vasoactive medications is anticipated to support circulation during induction, although it is acceptable in some patients to deliver vasoactives through a reliable peripheral intravenous line that is visible to the clinician's eye to monitor for infiltration while planning for a central venous catheter to be placed immediately after the induction of general anesthesia. The central venous catheter can also be used for central venous oxygen saturation monitoring as a surrogate for tissue oxygenation extraction and a proxy for mixed venous oxygenation, which is otherwise more accurately derived at the level of the PA.

In patients without PH or RV dysfunction undergoing noncardiac surgery, a PAC is generally not warranted on the basis of results of prospective studies in critically ill and surgical patients that have failed to demonstrate any benefit on morbidity or death.[103–105] Placement of a PAC is not without risks; it can induce arrhythmias, right bundle-branch block, complete heart block in patients with an existing left bundle-branch block, and, rarely, pulmonary arterial branch rupture during flow-directed advancement.[106–108] Of note, PA pressures will remain elevated in PH even when RV function, RAP, and cardiac index are optimized. Thus, PA pressures may not reflect that a patient with PAH has achieved low-risk status and poorly correlate with RV performance and perioperative risk if these other parameters have been optimized. We also recommend understanding the patient's LV systolic and diastolic function before augmenting pulmonary vasodilation to avoid high-output physiology from the RV, which may compound PH attributable to left-sided heart disease to worsen lung injury from pulmonary congestion. Central venous catheter data can be useful in the immediate postoperative period for monitoring of RAP and central venous oxygen saturation (which correlates with cardiac index) to guide titration of fluids, diuretics, and vasoactive medications. Although there are undeniable diagnostic benefits of PAC in the PH population, including accurate and real-time assessment of hemodynamic parameters in the inpatient or ICU setting, the

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benefit of perioperative PAC use has yet to be demonstrated in noncardiac surgery.[109,110]

Anesthesia Management

Hemodynamic stability during induction of anesthesia with the primary goal of preventing RV dysfunction is of utmost importance to avoid well-described catastrophic intraoperative events.[111–113] The choice of general or neuroaxial anesthesia, regional/peripheral nerve block with monitored anesthesia care, or a combination of anesthesia types is specific to the procedure and patient.[99,114–119] Appropriate monitoring, prompt mitigation of anesthesia-induced hemodynamic effects, pain control, and the presence of an anesthesiologist with expertise in managing PH and RHF and performing transesophageal echocardiography if necessary are more important than anesthetic type.[63,76,88,96,99,100,115,120–126] Additional surgery-specific risks (not directly related to the anesthetic type) that may need to be mitigated to prevent RHF should be considered. These include laparoscopic (hypercarbia and pneumoperitoneum) and orthopedic (risk for bleeding and embolism) surgeries, surgeries requiring extreme positioning (steep Trendelenburg or proning positions), one-lung ventilation (hypoxia, hypercarbia, increased airway pressures), or significant intravascular volume expansion for perioperative resuscitation.[76]

Peripheral VA ECMO as a rescue for potential postinduction intraoperative cardiac arrest may be considered on a case-by-case basis, depending on the severity of PH and RV dysfunction and ultimate goals of care.[111,113,127] In such situations, preemptive preinduction placement of small-caliber venous and arterial sheaths may expedite emergency ECMO cannulation, which is often lifesaving but not without risk of complications. For nonurgent, nonemergency operations, the discussion to use peripheral VA ECMO in line with patient goals of care should include all members of the multidisciplinary team, including the patient, caregiver(s), primary surgeon, ECMO specialists (perfusion team and proceduralists who place peripheral ECMO cannulas), anesthesiologist, and PH specialist.

General Anesthesia

During the perioperative period, the core hemodynamic goals are preserving RV function and maintaining end-organ perfusion. Anesthetic induction can be associated with significant hemodynamic changes that can lead to acute RHF. There have been no comparative studies on optimal induction agents in patients with PH. Etomidate (0.15–0.3 mg/kg) has minimal effect on systemic and PVR, heart rate, and contractility.[128] It remains controversial whether the known inhibitory effect on adrenocortical enzyme 11β-hydroxylase increases postoperative morbidity and death, although a recent meta-analysis did not report any association after a single induction dose.[129] Nevertheless, a continuous infusion or repetitive administration of etomidate can significantly increase morbidity and death and therefore must be avoided.[130] Ketamine is associated with an increase in PVR in adults and is therefore best avoided if PVR monitoring or pulmonary vasodilation is not concomitantly used.[131] Propofol can directly or indirectly adversely affect RV contractility[132,133] and should be used with caution because it may require subsequent or simultaneous administration of a vasopressor or inotrope. Opioids, when administered alone, have minimal effects on pulmonary circulation and reduce response to sympathetic stimulation, but they may induce unfavorable bradycardia in larger doses. Premedication with benzodiazepines and opioids should be performed judiciously; their coadministration may cause an acute increase in PA pressures attributable to hypoxia and hypercarbia (respiratory acidosis). A common option is to perform a rapid sequence induction with mask ventilation to minimize periods of hypercarbia and hypoxia that would cause significant RV afterload increase. It is important to allow sufficient exhalation time during mask ventilation because high intrathoracic pressure will cause an acute reduction in preload and subsequent severe hypotension. Succinylcholine (1–1.5 mg/kg) or rocuronium (1.2 mg/kg) offers the fastest onset of neuromuscular blockade in this setting.[134] Fentanyl (1–2 μg/kg) and lidocaine 50 to 100 mg IV are useful to blunt increases in sympathetic tone during laryngoscopy.[135,136] Any inhalational agent can be used for anesthetic maintenance except for nitrous oxide because of its effect on increasing PVR.[137] There is a dearth of comparative data on the effects of other commonly used inhalational agents on PVR, and one agent is not strongly favored over another.[138–140] If total intravenous anesthesia is chosen, then an infusion of propofol (50–150 $\mu g \cdot kg^{-1} \cdot min^{-1}$) with or without an opioid can be used.

Once the airway is secured, ventilation goals revolve around the avoiding hypoxia, favoring mild hypocarbia (30–35 mm Hg), and avoiding high inspiratory pressures and PEEP, which may compromise venous return, reduce cardiac output, increase PVR, and worsen RV function.[95] Any of the usual modes of ventilation available can be used because there is no evidence to support one mode over another. After lung recruitment to minimize atelectasis, hypoxia should preferentially be managed with an increase in fraction of inspired oxygen over a further increase in PEEP to avoid worsening RV afterload.[63]

Neuroaxial and Other Regional Techniques

In general, a single-shot spinal bolus should be avoided[88,141] because it can lead to a decrease in MAP and bradycardia from blockade of the cardioaccelerator fibers (that emanate from T1 to T4 levels), both of which can compromise RV function.[142] Continuous spinal anesthesia with slow titration of local anesthetic has been described as an alternative option in the obstetric population, but it is not widely used.[143] For neuroaxial technique, an epidural is more easily titrated to prevent an

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acute reduction in SVR. Vasopressor infusion should be readily available to counteract the sympatholytic effect of neuroaxial anesthesia, and care should be taken to avoid excessive fluid administration. Whenever possible, strong consideration should be given to performing a procedure under peripheral nerve block with minimal or no sedation.

Obstetric Anesthesia

Because of its high mortality rate, pregnancy is generally discouraged in patients with PH. Some patients are initially diagnosed with PH at the time of pregnancy and are at higher risk for morbidity and death.[144] Endothelin receptor antagonists and riociguat (pregnancy category X) are contraindicated in pregnancy because of a risk of birth defects, although PDE5 inhibitors and prostacyclin pathway agonists (pregnancy category B) are considered safe.[10] A parenteral prostacyclin may be preferred in pregnancy because of the ability to easily titrate the medication, especially with the hemodynamic changes that occur in the second and third trimesters and with delivery.[145] No prospective studies have compared epidural, spinal, or combined spinal-epidural with general anesthesia, and all approaches have been described in case reports and series.[117,141,143,146–155] Obstetric care for patients with PH should be performed at specialized PH centers with experienced anesthesia and obstetric teams. A multidisciplinary team involving an experienced obstetrician, PH specialist, and anesthesiologist is imperative in the management of obstetric patients with PH. Invasive monitoring (arterial and central venous catheters) with carefully titrated neuroaxial anesthetic (epidural) and low-dose vasopressors (eg, norepinephrine or vasopressin) titrated to maintain MAP at or above baseline, with inotrope and pulmonary vasodilator readily available in case of hemodynamic deterioration and need for RV support, is advised.[145] For parturients on long-term anticoagulation, an anticoagulation plan should be developed well in advanced of the due date for the peridelivery period, which usually involves therapeutic dosing of low-molecular-weight heparin with cessation for at least 24 hours before a planned delivery and resumption after delivery according to accepted guidelines.[156] In general, the timing of delivery should be controlled (not natural labor), with a vaginal birth with assisted delivery usually associated with fewer hemodynamic changes and less blood loss, whereas a cesarean section can avoid a potential lengthy labor that can result in labor-induced acidosis.[145] There is little evidence that cesarean section is superior to vaginal delivery because, although it avoids negative hemodynamic changes, it is associated with hypotension with induction of regional anesthesia and higher rates of hemorrhage and infection.[157] The postdelivery period can be the highest risk because of fluid shifts that can result in RHF; during this time, it is critical to ensure end-organ perfusion and brisk urine output, with appropriate use of PAH-targeted therapies, diuretics, and vasoactives as required.[145] An RV-centered approach to management, with optimization of risk status, an individualized approach to mode of anesthesia and delivery, and close follow-up, can result in good outcomes.[158]

Intraoperative PH Treatment

Patients who are already on parenteral PH treatment should continue therapy intraoperatively.[88,99] The central line used for delivery of parenteral prostacyclins should not be flushed because that can bolus the patient with drug, leading to hypotension and other side effects. Patients on subcutaneous treprostinil infusion can use a stable site for the infusion[159] of their drug away from the surgical field, or the subcutaneous route of medication administration should be transitioned to parenteral therapy before surgery. In most cases, the dose of prostacyclin does not need to be changed intraoperatively, but in some cases, uptitration or initiation of parenteral prostacyclin may be necessary to manage worsening PH with RHF. If that does occur, the higher dose of prostacyclin should be continued in the immediate postoperative period to ensure hemodynamic stability and to aid in RV recovery.

Sildenafil is available for intravenous administration, but as with other selective pulmonary vasodilators, it is indicated for group 1 PH and should be used with caution in non–group 1 PH. A 10-mg IV bolus may be administered once before surgery and up to 3 times per day until the patient is able to tolerate oral medications. Intravenous sildenafil may be considered in patients who cannot take oral medications, who have been on oral PDE5 inhibitors preoperatively, and who are not on simultaneous nitrate therapy.[160] Although dosing for preinduction oral sildenafil (50 mg) has been used successfully to reduce PVR and PA pressures in patients with PH undergoing valve surgery without a significant effect on MAP,[161] we do not recommend its routine use because it has been associated with worse long-term outcomes in outpatients with corrected valvular disease.[23]

Selective Pulmonary Vasodilators

NO and epoprostenol are selective pulmonary vasodilators that are most often used in noncardiac surgery.[162–165] NO can be delivered at a dose of 1 to 80 ppm, although most centers use maximum doses of 20 to 40 ppm.[166] Inhaled epoprostenol (iEPO) is the aerosolized formulation of epoprostenol solution and is commonly delivered in doses between 10 and 50 $ng \cdot kg^{-1} \cdot min^{-1}$. The efficacy and safety profiles of NO and iEPO are comparable in many small, observational studies, but the cost of procuring NO remains higher than that for iEPO.[167,168] Both epoprostenol and NO display short half-lives, which makes these agents appealing in the perioperative period when hemodynamic goals could be rapidly changing. However, the high price point of NO has led to reduced use of this medication in favor of cost-saving alternatives such as

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iEPO. In a recent single-center randomized clinical trial in 201 adult patients undergoing lung transplantation, iEPO was similar to inhaled NO in the development of postoperative severe primary graft dysfunction (44.7% in the iEPO group versus 39.8% in the NO group). This led to a point estimate risk difference of 4.9%, which was included within the prespecified 19% margin to demonstrate clinical equivalence.[169] In this same study, secondary outcomes of mechanical ventilation duration, hospital and ICU length of stay, death up to 90 days, and acute kidney injury incidence and grading were also similar between those that received iEPO and patients who received NO (P>0.05). As a secondary hemodynamic end point, daily mean pulmonary arterial pressures were measured and found to be similar between allocated treatment groups for the time that patients remained on treatment.[169] In addition, the potential for formation of potentially toxic products related to NO use (peroxynitrate, nitrogen dioxide, and methemoglobin)[96,170,171] has been determined not to be clinically important.[169]

Although NO has previously required expensive specialized delivery systems, the recent advent of additional NO manufacturers has altered market dynamics to lower its cost of procurement. It is important to note that cost-effectiveness analyses are needed that will meaningfully combine the differences in total costs associated with each agent with that of health outcomes to provide the incremental cost of each drug per incremental occurrence of the health outcome of interest.

Of note, NO and epoprostenol can each inhibit platelet aggregation as demonstrated in ex vivo studies.[161,172] A recent prospective clinical study has studied bleeding in 220 trial participants who had received either NO (107 patients, 49%) or iEPO (113 patients, 51%) to prevent RV failure after surgical treatment for advanced heart failure.[173] In this study, with the use of prespecified variables predictive of postoperative bleeding, no differences in bleeding class (previously developed and validated[174]) were seen between groups in either univariable (odds ratio, 1.08 [95% CI, 0.65–1.81]) or multivariable (odds ratio, 1.14 [95% CI, 0.60–2.17]) proportional odds models. Thus, no differences were seen in perioperative bleeding between iEPO and NO after these operations.

Vasopressors and Inotropes

There are no comparative studies between available inotropes and vasopressors in patients with PH, and recommendations are based on expert opinions and clinical experience. Norepinephrine and vasopressin are generally preferred over phenylephrine, which can cause unopposed pulmonary vasoconstriction, increased PVR, and reflex bradycardia.[88,175] Animal data suggest that vasopressin has minimal effects on PVR compared with other vasopressors.[176,177] High doses of vasopressin (>0.08–0.1 U/min) should be avoided because of the possible effect on coronary vasoconstriction, which may induce RV ischemia.[178,179] The inodilator subclass of inotropes may include milrinone (bolus of 25–50 μg/kg over 15 minutes, 0.25–0.75 $\mu g \cdot kg^{-1} \cdot min^{-1}$ infusion) and dobutamine (2.5–10 $\mu g \cdot kg^{-1} \cdot min^{-1}$), which can be used to improve RV contractility and to reduce RV afterload.[180–184] Both milrinone and dobutamine have inotropic, systemic, and pulmonary vasodilator effects and may lead to severe systemic vascular hypotension, requiring the addition of a vasopressor such as norepinephrine or terlipressin to maintain an adequate MAP. However, vasopressors may have a counterproductive effect and may increase PVR, which could limit the incremental benefit of PAH-targeted therapies. Therefore, before initiating inodilator therapy, perioperative clinicians need to carefully weigh risks versus benefits and ambitiously address intravascular volume expansion in resuscitation and bleeding treatment. Furthermore, bolusing milrinone can cause significant systemic hypotension and therefore should be avoided in patients with hypovolemia or hypotension. Notably, both inodilators can also induce arrhythmias. Last, epinephrine has several unfavorable effects, including tachycardia, arrhythmias, increased myocardial oxygen consumption, and a potentially dose-dependent increase in PVR. However, unlike milrinone and dobutamine, epinephrine does not induce a decrease in SVR and is an appropriate inotrope choice in the setting of systemic hypotension.[185]

Special Circumstances

Emergency Surgery

Patients undergoing emergency surgery face the highest perioperative risks. A recent literature review found a 15% to 50% 30-day mortality rate[5] in this population undergoing noncardiac, nonobstetric surgery. The main tenets of management for emergency surgery mirror those underlying critical care of the patient with PH: preload optimization, RV afterload reduction, and maintenance of RV coronary perfusion.[80,186] Diuretics and inotropy are used to restore optimal RV preload and contractility. RV afterload is reduced with the most pulmonary-selective vasodilators: NO and inhaled prostanoids. These agents are useful in acutely reducing PVR without significantly affecting SVR.[187,188] Efforts to normalize serum hemoglobin levels, arterial blood pH, oxygenation, and lung volumes on positive pressure can stave off acute increases in PVR. Aggressive treatment of pain, which can acutely stress pulmonary vascular tone if left untreated, is also important.[63,76] Preservation of a low PVR:SVR ratio is an important objective because RV coronary perfusion occurs equally in systole and diastole. This may mandate higher-than-normal MAP goals in a PH crisis through the use of vasopressors and, at times, continuous PAC monitoring. In some cases, emergency surgeries in otherwise

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viable patients with PH prompt the mobilization of ECMO and lung transplantation teams.

Congenital Heart Disease

Patients with corrected and uncorrected congenital heart disease can pose unique challenges in perioperative management. Like the PH population, patients with adult congenital heart disease are increasingly undergoing noncardiac surgery and are at higher risk for perioperative morbidity and death.[189] Congenital heart disease complicated by PH and Eisenmenger syndrome is associated with increased risks of perioperative complications. In a cohort of 24 patients with Eisenmenger syndrome who underwent 28 noncardiac surgeries between 1988 and 1996, perioperative mortality rate was 7%.[39] A more recent cohort of 33 patients with Eisenmenger syndrome undergoing 53 noncardiac surgeries reported systemic hypotension in 26%, oxygen desaturation in 17%, and a 30-day mortality rate of 3.8%.[48] The management of each patient with congenital heart disease depends on their specific physiology. Patients with single-ventricle/Fontan physiology are dependent on passive venous return, so it is important to maintain preload and to avoid increased PVR through avoidance of high PEEP and high intrathoracic pressure.[190] For those with shunts, it is important to prevent increased right-to-left shunting, which can occur even in patients with a basal left-to-right shunt, because such shunting can cause a downward spiral of hypoxemia, acidosis, and systemic hypotension.[191] In these patients, maintaining a low PVR:SVR ratio by avoiding increases in PVR and decreases in SVR, as well as maintaining contractility, preload, and cardiac output, is critical.[190] There are many other considerations in this patient population not specifically relevant to PH that are beyond the scope of this scientific statement.

POSTOPERATIVE MANAGEMENT OF PH

Surveillance in the Postanesthesia Care Unit

After routine surgery without untoward intraoperative events, most patients with PH are admitted to the postanesthesia care unit. During this time, standard American Society of Anesthesiology monitoring of oxygen levels (with pulse oximetry to avoid hypoxia), end-tidal carbon dioxide levels (to avoid hypercarbia), and blood pressure (to avoid cardiovascular hypoperfusion) is performed. Acute incisional pain from surgery or postdelivery autotransfusion from uterine contractions can increase preload, venous hypertension, PVR, and SVR, which may lead to acute cardiovascular decompensation and cardiac arrest. Thus, optimizing pain control before leaving the operating room for patients with PH who have been extubated from general endotracheal anesthesia is a key principle for promoting early and safe recovery from elective noncardiac surgery. If a patient with PH has undergone general anesthesia and presents to the postanesthesia care unit, a thorough review of their history for reactive airway disease should be performed. Wheezing or rhonchi may be a sign of worsening bronchoconstriction, which should be avoided because it can contribute to difficulty with ventilation, rising PVR, and impending RHF. Patients with obesity, PH, and obstructive sleep apnea who have received opioids are at an especially high risk for cardiopulmonary decompensation and should be closely monitored after noncardiac surgery.[192]

Critical Care Management of Patients With PH at Risk for RV Failure

Patients with low disease severity and perioperative risk and patients who undergo low-risk ambulatory surgical procedures rarely experience perioperative events that require inpatient hospitalization. As discussed previously, following predetermined perioperative risk stratification pathways that have been planned by health care professionals most familiar with the patient is paramount to the safe passage of patients with PH through the perioperative period.[62] Thus, it essential for the perioperative clinical team to be involved in the planning phase for this patient cohort (Figure 2). In cases when the complexity of the operation is apparent during the planning phase or the severity of pulmonary vascular disease progression for the patient requires close monitoring after surgery beyond what it available in telemetry or ward units, then admission to the ICU in a planned, elective manner is preferred. This ensures that all resources, invasive monitoring, medications, and personnel are deployed for optimal critical care management.

Conversely, the patient will assuredly benefit from ICU admission after surgery if intraoperative events have resulted in hemodynamic compromise, if the patient required escalation in medical therapy and placement of invasive monitoring, or if the patient would benefit from additional pulmonary support by remaining on mechanical ventilation into the early postoperative period. In more extreme cases, ICU admission could be required if intraoperative cardiopulmonary decompensation results in the need for mechanical circulatory support. The pathophysiology of PH-induced RHF has been discussed; the following sections address ICU monitoring and medical and procedural management of this devastating condition.

Invasive and Laboratory Monitoring

In the ICU, monitoring is similar to that performed in the operating room. Although discussion of specific ICU monitors that could aid in management of patients with PH is beyond the scope of this document, goal hemodynamic values should be focused on end-organ function

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and biomarkers of perfusion. For ICUs that are developing protocols for bedside monitoring to alert clinicians of critical values, general triggered alerts could include cardiac index <2.2 $L \cdot min^{-1} \cdot m^{-2}$, Sv_{O_2} <55%, and urine output <0.5 $cm^3 \cdot kg^{-1} \cdot h^{-1}$ for 2 consecutive hours. Although echocardiography is useful for evaluating RV function in the ICU, the complementary nature of invasive hemodynamic monitoring with cardiovascular and pulmonary imaging (eg, ultrasonography, chest radiograph) can improve the clinician's ability to diagnose and manage. In the acute ICU setting, qualitative TTE assessments can be performed that include RV:LV size ratio in the 4-chamber view, interventricular dependence and synchrony for optimizing loading conditions and stroke volume, the presence of tricuspid regurgitation and determination of tricuspid valve regurgitation degree, and space-occupying collections that may provide reversible causes of obstructive shock (eg, pericardial effusion, abdominal ascites, tension pneumothorax, pulmonary embolus). In addition, bedside assessment of RV-to-pulmonary vascular coupling shows promise as continuous monitoring of patients with PH-induced RHF and subsequent monitoring of recovery after treatment.[193]

PH-induced RHF may lead to visceral organ venous congestion attributable to venous hypertension and organ hypoperfusion caused by low cardiac output syndrome. Thus, serial monitoring of liver (aspartate transaminase, alanine transaminase, bilirubin) and renal (urinary catheter, creatinine kinetics and glomerular filtration rate, electrolyte balance) function is important. Although the exact goal fluid balance for PH-induced RHF can vary from moment to moment in the ICU, a net negative fluid balance is generally a recommended starting point. This means that the total fluid measure into the patient will be less than the total fluid measure that is drained from the patient in a specific time frame, which is usually a 12- or 24-hour period. In addition, biomarkers that are clinically available such as lactate could provide supportive evidence of hypoperfusion that requires additional management. However, reliance on any single laboratory or hemodynamic biomarker to guide management is not advised.

Medical Management of PH-Induced RHF After Noncardiac Surgery

In conjunction with PAH therapies, inotropes are the hallmark of medical management in the event of cardiogenic shock from RHF and are used to augment RV myocardial contractility. To promote RV-to-PA coupling in the acute care setting, inhaled pulmonary vasodilators can selectively lower PVR in patients with PH who display vasoreactivity (reversibility of high PVR) through pulmonary-selective vasodilation (through NO or iEPO, as described previously).[166] Inhaled prostacyclins may also include iloprost, which may be administered in the postoperative period with the recognition that the half-life of this medication is ≈30 minutes compared with NO (half-life is seconds) and epoprostenol (half-life is a few minutes).

Milrinone may also be helpful in PH-induced RHF management after noncardiac surgery. However, its vasodilatory properties could compound hypovolemia in the immediate postoperative period to lower systemic blood pressure and to reduce RV perfusion and contractility. Thus, the use of this type 3 phosphodiesterase inhibitor is recommended along with a vasopressor with inotropic properties (epinephrine, norepinephrine) or vasopressor alone (vasopressin). With this in mind, inhaled milrinone has also been described as an alternative inhaled pulmonary vasodilator agent[194] but has been described and systematically reviewed mainly in critically ill patients after cardiac operations.[195] Once patients with PH have been stabilized in the postoperative period, scheduled oral, inhaled, or parenteral agents may be initiated in consultation with a PH specialist.

Vasoactive medications should promote cardiovascular function and maintain end-organ perfusion. Declining urine output and early changes in estimated glomerular filtration rate consistent with acute kidney injury often herald the need for diuretics or renal replacement therapy to avoid volume overload and worsening visceral organ venous congestion. Fluid shifts can occur well after the postoperative period and can be particularly challenging to manage in the setting of RHF. This may necessitate intravenous fluids early in the postoperative course to maintain adequate filling pressures followed by later diuresis to deal with fluid shifts from the interstitium back to the intravascular space. Invasive monitoring and echocardiography are recommended to gauge cardiac loading conditions. For patients with PH and end-stage renal disease admitted to the ICU, nephrology consultation is essential to facilitate timely renal replacement therapy. Metabolic acidosis and hyperkalemia attributable to hypoperfusion with acute kidney injury may also impair cardiovascular performance and synergistically, with an acid-base imbalance, precipitate the need for renal replacement therapy. Despite early interventions, death remains high for critically ill patients with PH (precapillary PH in particular) and renal disease.[196] Thus, early family discussions of goals of care are recommended to develop realistic expectations for patients who are not incapacitated on life support devices and are able to participate in their own decision-making and for caregivers.

Additional Treatment Modalities

Mechanical ventilation through endotracheal intubation may be essential to deliver adequate oxygen for organ protection and to avoid hypoxic pulmonary vasoconstriction while patients with PH are critically ill. Noninvasive ventilation (eg, bilevel positive airway pressure or high-flow oxygen) should be considered in all extubated

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patients with concern of hypoxemia to avoid worsening RHF, respiratory failure, and PH crisis. A study of >21 000 patients with PH reviewed through the National Inpatient Sample (2006–2012) indicated that patients with PH who underwent invasive mechanical ventilation had higher death compared with patients with PH who underwent noninvasive ventilation (39.1% versus 12.6%; $P<0.001$) and longer hospital stays than those who experienced noninvasive mechanical ventilation (12 days [interquartile range, 6 to 22 days] versus 7 days [interquartile range, 3 to 12 days]; $P<0.001$).[197] However, should the need for invasive mechanical ventilation develop, the decision to intubate should be made as early as possible to avoid further risk of cardiovascular collapse. This can be performed by airway specialists (perioperative anesthesiology care team) from the operating room or an intensive care team with capabilities to intubate quickly. Intubation may require the administration of intravenous medications to support RV hemodynamic goals to avoid cardiovascular collapse. Patients undergoing intubation may develop the Bezold-Jarisch reflex with reflex bradycardia and hypotension; this may require treatment with adrenergic agents.[198] If there is high-risk PH with worsening RHF or imminent cardiac collapse, then the ECMO team should be on standby during intubation. There should be a family discussion if time allows of the poor prognosis related to the occurrence of intubation and invasive mechanical ventilation in these patients.

Because the constellation of sedative medications and muscle relaxants can eliminate sympathetic drive, inotropes and vasopressors are recommended as adjuncts to the induction of anesthesia for urgent or emergency endotracheal intubation. Although each ICU may have a different sedation protocol, maintenance of anesthesia during mechanical ventilation should include evidence for reversal of muscle paralysis before the intravenous sedative medication dosing is reduced to allow comfortable, light sedation so that the patient is able to be alert while calm when neurological assessment checks are performed (Richmond Agitation Sedation Scale, 0 to −2). Although no specific ventilation strategy has been described in this population that could improve outcomes, pulmonary-to-ventilator synchrony is essential for optimizing synchrony between right-sided heart venous return and left-sided heart cardiac output through stabilized hysteresis of inspiratory and expiratory intrathoracic pressures. Meanwhile, blood oxygen-carrying capacity assessed by measured hemoglobin values can be goal directed according to unit protocols, Svo_2, and tissue perfusion monitoring if available.

Temporary Mechanical Circulatory Support in the ICU

If medical therapy proves inadequate to preserve cardiovascular function for end-organ perfusion, mechanical circulatory support is often discussed with the family, intensive care team, perfusion services, and procedural team (if different from the intensive care and surgical teams) who will cannulate peripheral vessels for intra-aortic balloon pump (IABP) counterpulsation, venovenous (VV) ECMO, VA ECMO, or RV assist device insertion.

Intra-aortic balloon pump counterpulsation has become more prevalent in RV dysfunction, especially in the setting of patients with left-sided ventricular dysfunction. The physiological relevance derives from improved coronary perfusion, which can improve cardiac output and blood pressure. This improved cardiac output can reduce the left atrial pressure and improve forward blood flow from the RV. However, use as a primary modality for management of RHF from PH is not recommended.[199]

VV ECMO is often used to achieve adequate oxygenation or ventilation (carbon dioxide removal), to reduce PVR, and to eliminate the strain on the RV. However, VV ECMO requires a normal-functioning RV in the setting of a primary pulmonary disorder. Thus, VV ECMO for PH-induced RHF can be used for acute respiratory distress and lung injury in the setting of high-dose vasopressors and inotropes[200] with the understanding that VV ECMO does not directly address RV decompensation. If RHF persists after VV ECMO deployment, an arterial cannula may be placed to aid in circulatory support, thus changing the cannula configuration to veno-arterio-venous ECMO. In this configuration, deoxygenated blood enters the ECMO circuit, and oxygenated blood returns to the PA (circumventing the right side of the heart) and to the arterial cannula for circulatory support. The fraction of blood that enters the PA versus the fraction that enters the arterial circulation can be adjusted and dialed in with an inline flowmeter.

VA ECMO for RHF refractory to medical therapy would be the usual mechanical support modality deployed in an emergency situation after cardiac arrest in the operating room, postanesthesia care unit, or ICU. This modality can serve as a bridge to decision-making, particularly if a reversible cause for cardiogenic shock is discovered (eg, intraoperative pulmonary embolus, venous air embolism, acute RV myocardial infarction requiring cardiac catheterization). With peripheral cannulation (commonly through femoral insertion of venous and arterial vessels), there is the risk that improved RV function with ongoing pulmonary injury could result in ejection of deoxygenated blood from a normal functioning LV and subsequent delivery of deoxygenated blood to the heart and brain through coronary and great vessels, respectively, referred to as north-south syndrome. This syndrome can be monitored by assessment of arterial blood gases from a right upper extremity arterial line. If cardiac function has improved with persistent lung injury, transition to VV ECMO is warranted. If there is no lung injury but there is persistent RHF, then a percutaneous RV assist device can be placed to aid in ICU rehabilitation.[201]

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KNOWLEDGE GAPS AND RESEARCH PRIORITIES

Given the scarcity of the data on the perioperative management of PH, multiple knowledge gaps exist that could be addressed through future studies such as the ability to correctly identify patients with PH at risk for adverse perioperative outcomes and surgical procedures that confer the highest risks. The prevalence of all 5 WSPH groups combined is significantly higher in the general population than the prevalence of its rare forms such as idiopathic or hereditary PAH. However, studies on perioperative risks in patients with group 2 and 3 PH, which account for most PH cases, are lacking. It is expected that the presence of left-sided heart disease in group 2 PH imposes an increased risk for hemodynamic compromise just as there is an increased risk in patients with heart failure undergoing surgery. On the other hand, patients with group 3 PH are most likely at risk of developing pulmonary complications such as respiratory failure and pneumonia during or after a surgical procedure, which can lead to further RV decompensation. Available data suggest that the overall perioperative risk in non–group 1 PH is increased but less than in patients with group 1 PH,[6] although an accurate identification of risk factors that differentiate these groups is lacking. Armed with the knowledge that RHF is a common perioperative complication in patients with PH, clinicians should focus on supporting the RV function during the surgical procedure and in the following 48 to 72 hours, when the risk for decompensation is the highest. However, there is no guidance on when to consider preconditioning the RV with short-term prostacyclin therapy preoperatively or to use ECMO support to alleviate the risk of RHF during a surgical procedure. Experience from large centers and prospective reports may help elucidate the role of RV support, especially in patients with advanced PH. Prospective, multicenter registries enrolling patients with PH from specialized PH centers could also help identify differences in outcomes among the 5 WSPH groups, refine the risk factors specific for each PH group, and tailor a more individualized approach that is based on the type of PH and complexity of the surgical procedure.

ARTICLE INFORMATION

The American Heart Association makes every effort to avoid any actual or potential conflicts of interest that may arise as a result of an outside relationship or a personal, professional, or business interest of a member of the writing panel. Specifically, all members of the writing group are required to complete and submit a Disclosure Questionnaire showing all such relationships that might be perceived as real or potential conflicts of interest.

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Disclosures

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*Modest.

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*Modest.

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